

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L4	1	10/701331	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/04/13 13:40
L5	14	Cines Douglas	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 13:40
L6	13	Poncz Mortimer	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 13:40
L7	52	u-PA platelet	US-PGPUB; USPAT; EPO; JPO; DERWENT	SAME	ON	2006/04/13 13:41
L8	53	PF4 promoter	US-PGPUB; USPAT; EPO; JPO; DERWENT	SAME	ON	2006/04/13 13:45
L9	1	I7 and I8	US-PGPUB; USPAT; EPO; JPO; DERWENT	SAME	ON	2006/04/13 13:42
L10	14	u-PA PF4	US-PGPUB; USPAT; EPO; JPO; DERWENT	AND	ON	2006/04/13 13:42
L12	7453	platelet factor	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 13:44
L13	6	urokinase-type plasminogen activator-initiated	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 13:44
L14	1626	urokinase plasminogen	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 14:12
L15	217	I12 and I14	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 13:44
L16	6	(I12 and I14).clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 13:44
L17	5	platelet factor promoter	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 13:45

## EAST Search History

L18	346	l14 and thrombus	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 14:13
L19	1	l18 and l8	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 14:13
L20	2	l14 and l8	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2006/04/13 14:13

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(FILE 'HOME' ENTERED AT 14:13:40 ON 13 APR 2006)

FILE 'MEDLINE, SCISEARCH, CAPLUS, BIOSIS' ENTERED AT 14:13:57 ON 13 APR 2006

L1 3295 S (PLATELET (3W) PROMOTER) OR (PF4 (L) PLATELET)  
L2 23170 S U-PA OR (UROKINASE?(5W)PLASMINOGEN (5W)ACTIVAT?)  
L3 5 S L1 (L) L2  
L4 2 DUP REM L3 (3 DUPLICATES REMOVED)  
L5 6 S L1 AND L2  
L6 3 DUP REM L5 (3 DUPLICATES REMOVED)  
E CINES DOUGLAS?/AU  
L7 252 S E2  
E PONCZ MORTIMER?/AU  
L8 206 S E2  
L9 412 S L7 OR L8  
L10 77 S L9 AND L2  
L11 4 S L10 AND L1  
L12 2 DUP REM L11 (2 DUPLICATES REMOVED)

=> d ti so au ab pi l12 1-2

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Cells of hematopoietic lineage transformed with vectors comprising cell-specific promoters and transgenes encoding fibrinolytic proteins, and their use in treatment of vascular injuries, such as preventing thrombus formation  
SO U.S. Pat. Appl. Publ., 22 pp.  
CODEN: USXXCO  
IN Cines, Douglas B.; Poncz, Mortimer  
AB The invention provides novel recombinant nucleic acid mols., host cells transformed/transduced/transfected with said mols., and methods for delivery of recombinant transgenes using modified cells of the hematopoietic lineage. The invention relates that said recombinant nucleic acid mols. are viral or non-viral vectors containing a sequence encoding a transgene under the control of a cell-specific promoter. The invention also relates that transformed cells of the hematopoietic lineage can be a secretory cell, and/or selected from a group including platelet, megakaryocyte, erythrocyte, neutrophil, eosinophil, monocyte, basophil, dendritic cell, mast cell, macrophage, and natural killer cell. The invention also provides that the transformed host cells containing the recombinant nucleic acid mol. are employed in methods for treating or preventing vascular injuries, such as thrombus formation. Specifically, the invention provides a method for treating or preventing thrombus formation in a patient by administering transformed host cells encoding a fibrinolytic protein, such as **urokinase plasminogen activator (u-PA)**, Factor VIIa, Factor VIII, Factor IX or fibrinogen. The disclosed materials and methods were demonstrated by creating transgenic mice that expressed **u-PA using platelet factor 4 gene promoter**. These transgenic mice were characterized and used to study the effect of ectopic expression of **u-PA** in platelets on thrombus development and stability. Specifically, the invention used the carotid artery injury thrombosis model, and reported that transgenic mice were resistant to the development of occlusive carotid artery thrombosis. The invention also reported transgenic mice displayed rapid resolution of pulmonary emboli.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI US 2004126885	A1	20040701	US 2003-701331	20031104

L12 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1

TI Antithrombotic thrombocytes: ectopic expression of **urokinase**  
-type **plasminogen activator** in platelets.

SO Blood, (2003 Aug 1) Vol. 102, No. 3, pp. 926-33. Electronic Publication:  
2003-04-10.  
Journal code: 7603509. ISSN: 0006-4971.

AU Kufrin Dubravka; Eslin Don E; Bdeir Khalil; Murciano Juan-Carlos; Kuo  
Alice; Kowalska M Anna; Degen Jay L; Sachais Bruce S; **Cines Douglas**  
**B; Poncz Mortimer**

AB Arterial occlusive disorders are a leading cause of human morbidity. We  
hypothesized that ectopic expression of fibrinolytic proteins in platelets  
could be used to favorably alter the hemostatic balance at sites of  
thrombosis. To test our hypothesis, we directed murine **urokinase**  
-type **plasminogen activator** transgene expression to  
platelets using a **platelet factor 4 promoter**.  
Urokinase was selectively expressed and stored in the platelets of these  
mice. These transgenic mice had altered platelet biology and a bleeding  
diathesis similar to that seen in patients with Quebec platelet disorder,  
affirming the role of ectopic urokinase expression as the etiology of this  
inherited disease. These mice were resistant to the development of  
occlusive carotid artery thrombosis in the absence of systemic  
fibrinolysis and displayed rapid resolution of pulmonary emboli.  
Moreover, transfusion of urokinase-expressing platelets into wild-type  
mice prevented formation of occlusive arterial thrombi. These studies  
show the feasibility of delivering fibrinolytic agents to sites of  
incipient thrombus formation through selective storage in platelets and  
offer a new strategy to prevent thrombosis and hemorrhage.